

SEQUENCE LISTING

<110> Davis, Samuel et al.

<120> Tie-2 Ligands, Methods of Making and Uses Thereof

<130> REG 330G1Z

<140> Not Yet Known

<141> Filed Herewith

<150> 09/442,717

<151> 1999-11-18

<150> 08/930,721

<151> 1998-03-10

<150> PCT/US96/04806

<151> 1996-04-05

<160> 6 *

<170> PatentIn Ver. 2.0

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<211> 2149

<212> DNA

<213> Homo sapiens

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<222> (310)..(1803)

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Leu Pro Glu His Asp Gly Asn Cys Arg Glu Ser Thr Thr Asp Gln Tyr	
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aac agt tta tta gaa cat aaa atc tta gaa atg gaa gga aaa cac aag 927

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gtt act cgt caa aca tat ata atc cag gag ctg gaa aag caa tta aac 1023

Val Thr Arg Gln Thr Tyr Ile Ile Gln Glu Leu Glu Lys Gln Leu Asn

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aac cga gcc tat tca cag tat gac aga ttc cac ata gga aat gaa aag 1503
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Asp Asn Asp Asn Cys Met Cys Lys Cys Ala Leu Met Leu Thr Gly Gly

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tgg tgg ttt gat gct tgt ggc ccc tcc aat cta aat gga atg ttc tat 1695

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ttc aaa ggg ccc agt tac tcc tta cgt tcc aca act atg atg att cga 1791

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Pro Leu Asp Phe

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tggagccggtt tgagttcaca agagtctcta cttgggggtga cagtgtcac gtggctcgac 2023

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Glu His Asp Gly Asn Cys Arg Glu Ser Thr Thr Asp Gln Tyr Asn Thr

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Asn Ala Leu Gln Arg Asp Ala Pro His Val Glu Pro Asp Phe Ser Ser
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Gln Lys Leu Gln His Leu Glu His Val Met Glu Asn Tyr Thr Gln Trp
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Ala Gln Ile Gln Gln Asn Ala Val Gln Asn His Thr Ala Thr Met Leu
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Glu Ile Gly Thr Ser Leu Leu Ser Gln Thr Ala Glu Gln Thr Arg Lys
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Ile Gln Leu Leu Glu Asn Ser Leu Ser Thr Tyr Lys Leu Glu Lys Gln
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Leu Leu Gln Gln Thr Asn Glu Ile Leu Lys Ile His Glu Lys Asn Ser
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Leu Asp Thr Leu Lys Glu Glu Lys Glu Asn Leu Gln Gly Leu Val Thr
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Arg Gln Thr Tyr Ile Ile Gln Glu Leu Glu Lys Gln Leu Asn Arg Ala
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Thr Thr Asn Asn Ser Val Leu Gln Lys Gln Gln Leu Glu Leu Met Asp
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Thr Val His Asn Leu Val Asn Leu Cys Thr Lys Glu Gly Val Leu Leu
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Lys Gly Gly Lys Arg Glu Glu Glu Lys Pro Phe Arg Asp Cys Ala Asp
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Val Tyr Gln Ala Gly Phe Asn Lys Ser Gly Ile Tyr Thr Ile Tyr Ile
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Asn Asn Met Pro Glu Pro Lys Lys Val Phe Cys Asn Met Asp Val Asn
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Phe Gln Arg Gly Trp Lys Glu Tyr Lys Met Gly Phe Gly Asn Pro Ser
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Gly Glu Tyr Trp Leu Gly Asn Glu Phe Ile Phe Ala Ile Thr Ser Gln
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Arg Gln Tyr Met Leu Arg Ile Glu Leu Met Asp Trp Glu Gly Asn Arg
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Ala Tyr Ser Gln Tyr Asp Arg Phe His Ile Gly Asn Glu Lys Gln Asn
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Tyr Arg Leu Tyr Leu Lys Gly His Thr Gly Thr Ala Gly Lys Gln Ser
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Ser Leu Ile Leu His Gly Ala Asp Phe Ser Thr Lys Asp Ala Asp Asn
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Asp Asn Cys Met Cys Lys Cys Ala Leu Met Leu Thr Gly Gly Trp Trp
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Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Phe Tyr Thr Ala
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aaaatttttaa aatttttagaa caaagctaac aaatggctag ttttctatga ttctttcttca 180

aacgctttct ttgaggggga aagagtcaaa caaacaagca gttttacctg aaataaagaa 240

ctagtttttag aggtcagaag aaaggagcaa gttttgagag aggcacggaa ggagtgtgct 300

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Met Thr Val Phe Leu Ser Phe Ala Phe Leu Ala Ala Ile Leu

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ctt cca gaa cac gat ggc aac tgt cgt gag agt acg aca gac cag tac 495

Leu Pro Glu His Asp Gly Asn Cys Arg Glu Ser Thr Thr Asp Gln Tyr

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aac aca aac gct ctg cag aga gat gct cca cac gtg gaa ccg gat ttc 543
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tct tcc cag aaa ctt caa cat ctg gaa cat gtg atg gaa aat tat act 591
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 Gln Trp Leu Gln Lys Leu Glu Asn Tyr Ile Val Glu Asn Met Lys Ser

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aac agt tta tta gaa cat aaa atc tta gaa atg gaa gga aaa cac aag 927
 Asn Ser Leu Leu Glu His Lys Ile Leu Glu Met Glu Gly Lys His Lys
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gtt act cgt caa aca tat ata atc cag gag ctg gaa aag caa tta aac 1023
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atg gac aca gtc cac aac ctt gtc aat ctt tgc act aaa gaa gtt tta 1119
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gat gta tat caa gct ggt ttt aat aaa agt gga atc tac act att tat 1215
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 Ala Gly Gln Asn His Gly Lys Leu Asn Gly Ile Lys Trp His Tyr Phe
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Glu His Asp Gly Asn Cys Arg Glu Ser Thr Thr Asp Gln Tyr Asn Thr

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Asn Ala Leu Gln Arg Asp Ala Pro His Val Glu Pro Asp Phe Ser Ser

65 70 75 80

Gln Lys Leu Gln His Leu Glu His Val Met Glu Asn Tyr Thr Gln Trp

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Leu Gln Lys Leu Glu Asn Tyr Ile Val Glu Asn Met Lys Ser Glu Met

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Ile Gln Leu Leu Glu Asn Ser Leu Ser Thr Tyr Lys Leu Glu Lys Gln

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Glu Tyr Trp Leu Gly Asn Glu Phe Ile Phe Ala Ile Thr Ser Gln Arg
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Gln Tyr Met Leu Arg Ile Glu Leu Met Asp Trp Glu Gly Asn Arg Ala
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Tyr Ser Gln Tyr Asp Arg Phe His Ile Gly Asn Glu Lys Gln Asn Tyr
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Arg Leu Tyr Leu Lys Gly His Thr Gly Thr Ala Gly Lys Gln Ser Ser
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Leu Ile Leu His Gly Ala Asp Phe Ser Thr Lys Asp Ala Asp Asn Asp
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Asn Cys Met Cys Lys Cys Ala Leu Met Leu Thr Gly Gly Trp Trp Phe
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Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Phe Tyr Thr Ala Gly
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Gln Asn His Gly Lys Leu Asn Gly Ile Lys Trp His Tyr Phe Lys Gly
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<222> (357)..(1844)

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ccaagtgagc aggactgttc ttcccactgc aatctgacag ttactgcat gcttgagag 180

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cag agg gac gcg ccg ctc gaa tac gat gac tcg gtg cag agg ctg caa 599

Gln Arg Asp Ala Pro Leu Glu Tyr Asp Asp Ser Val Gln Arg Leu Gln

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gtg ctg gag aac atc atg gaa aac aac act cag tgg cta atg aag ctt 647

Val Leu Glu Asn Ile Met Glu Asn Asn Thr Gln Trp Leu Met Lys Leu

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gag aat tat atc cag gac aac atg aag aaa gaa atg gta gag ata cag 695

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gaa gcc caa gta tta aat cag acc acg aga ctt gaa ctt cag ctc ttg 839

Glu Ala Gln Val Leu Asn Gln Thr Thr Arg Leu Glu Leu Gln Leu Leu

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acc agt gaa ata aac aaa ttg caa gat aag aac agt ttc cta gaa aag 935

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Lys Val Leu Ala Met Glu Asp Lys His Ile Ile Gln Leu Gln Ser Ile	
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aaa gaa gag aaa gat cag cta cag gtg tta gta tcc aag caa aat tcc	1031
Lys Glu Glu Lys Asp Gln Leu Gln Val Leu Val Ser Lys Gln Asn Ser	
210 215 220 225	
atc att gaa gaa cta gaa aaa aaa ata gtg act gcc acg gtg aat aat	1079
Ile Ile Glu Glu Leu Glu Lys Lys Ile Val Thr Ala Thr Val Asn Asn	
230 235 240	
tca gtt ctt caa aag cag caa cat gat ctc atg gag aca gtt aat aac	1127
Ser Val Leu Gln Lys Gln Gln His Asp Leu Met Glu Thr Val Asn Asn	
245 250 255	
tta ctg act atg atg tcc aca tca aac tca gct aag gac ccc act gtt	1175
Leu Leu Thr Met Met Ser Thr Ser Asn Ser Ala Lys Asp Pro Thr Val	
260 265 270	
gct aaa gaa gaa caa atc agc ttc aga gac tgt gct gaa gta ttc aaa	1223
Ala Lys Glu Glu Gln Ile Ser Phe Arg Asp Cys Ala Glu Val Phe Lys	
275 280 285	
tca gga cac acc aca aat ggc atc tac acg tta aca ttc cct aat tct	1271
Ser Gly His Thr Thr Asn Gly Ile Tyr Thr Leu Thr Phe Pro Asn Ser	
290 295 300 305	
aca gaa gag atc aag gcc tac tgt gac atg gaa gct gga gga ggc ggg	1319
Thr Glu Glu Ile Lys Ala Tyr Cys Asp Met Glu Ala Gly Gly Gly Gly	
310 315 320	

tgg aca att att cag cga cgt gag gat ggc agc gtt gat ttt cag agg 1367

Trp Thr Ile Ile Gln Arg Arg Glu Asp Gly Ser Val Asp Phe Gln Arg

325

330

335

act tgg aaa gaa tat aaa gtg gga ttt ggt aac cct tca gga gaa tat 1415

Thr Trp Lys Glu Tyr Lys Val Gly Phe Gly Asn Pro Ser Gly Glu Tyr

340

345

350

tgg ctg gga aat gag ttt gtt tcg caa ctg act aat cag caa cgc tat 1463

Trp Leu Gly Asn Glu Phe Val Ser Gln Leu Thr Asn Gln Gln Arg Tyr

355

360

365

gtg ctt aaa ata cac ctt aaa gac tgg gaa ggg aat gag gct tac tca 1511

Val Leu Lys Ile His Leu Lys Asp Trp Glu Gly Asn Glu Ala Tyr Ser

370

375

380

385

ttg tat gaa cat ttc tat ctc tca agt gaa gaa ctc aat tat agg att 1559

Leu Tyr Glu His Phe Tyr Leu Ser Ser Glu Glu Leu Asn Tyr Arg Ile

390

395

400

cac ctt aaa gga ctt aca ggg aca gcc ggc aaa ata agc agc atc agc 1607

His Leu Lys Gly Leu Thr Gly Thr Ala Gly Lys Ile Ser Ser Ile Ser

405

410

415

caa cca gga aat gat ttt agc aca aag gat gga gac aac gac aaa tgt 1655

Gln Pro Gly Asn Asp Phe Ser Thr Lys Asp Gly Asp Asn Asp Lys Cys

420

425

430

att tgc aaa tgt tca caa atg cta aca gga ggc tgg tgg ttt gat gca 1703
 Ile Cys Lys Cys Ser Gln Met Leu Thr Gly Gly Trp Trp Phe Asp Ala
 435 440 445

tgt ggt cct tcc aac ttg aac gga atg tac tat cca cag agg cag aac 1751
 Cys Gly Pro Ser Asn Leu Asn Gly Met Tyr Tyr Pro Gln Arg Gln Asn
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 Thr Asn Lys Phe Asn Gly Ile Lys Trp Tyr Tyr Trp Lys Gly Ser Gly
 470 475 480

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 Tyr Ser Leu Lys Ala Thr Thr Met Met Ile Arg Pro Ala Asp Phe
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Ala Ala Tyr Asn Asn Phe Arg Lys Ser Met Asp Ser Ile Gly Lys Lys

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Gln Tyr Gln Val Gln His Gly Ser Cys Ser Tyr Thr Phe Leu Leu Pro

35 40 45

Glu Met Asp Asn Cys Arg Ser Ser Ser Ser Pro Tyr Val Ser Asn Ala

50 55 60

Val Gln Arg Asp Ala Pro Leu Glu Tyr Asp Asp Ser Val Gln Arg Leu

65 70 75 80

Gln Val Leu Glu Asn Ile Met Glu Asn Asn Thr Gln Trp Leu Met Lys

85 90 95

Leu Glu Asn Tyr Ile Gln Asp Asn Met Lys Lys Glu Met Val Glu Ile

100 105 110

Gln Gln Asn Ala Val Gln Asn Gln Thr Ala Val Met Ile Glu Ile Gly

115

120

125

Thr Asn Leu Leu Asn Gln Thr Ala Glu Gln Thr Arg Lys Leu Thr Asp

130

135

140

Val Glu Ala Gln Val Leu Asn Gln Thr Thr Arg Leu Glu Leu Gln Leu

145

150

155

160

Leu Glu His Ser Leu Ser Thr Asn Lys Leu Glu Lys Gln Ile Leu Asp

165

170

175

Gln Thr Ser Glu Ile Asn Lys Leu Gln Asp Lys Asn Ser Phe Leu Glu

180

185

190

Lys Lys Val Leu Ala Met Glu Asp Lys His Ile Ile Gln Leu Gln Ser

195

200

205

Ile Lys Glu Glu Lys Asp Gln Leu Gln Val Leu Val Ser Lys Gln Asn

210

215

220

Ser Ile Ile Glu Glu Leu Glu Lys Lys Ile Val Thr Ala Thr Val Asn

225

230

235

240

Asn Ser Val Leu Gln Lys Gln Gln His Asp Leu Met Glu Thr Val Asn

245

250

255

Asn Leu Leu Thr Met Met Ser Thr Ser Asn Ser Ala Lys Asp Pro Thr

260

265

270

Val Ala Lys Glu Glu Gln Ile Ser Phe Arg Asp Cys Ala Glu Val Phe
 275 280 285

Lys Ser Gly His Thr Thr Asn Gly Ile Tyr Thr Leu Thr Phe Pro Asn
 290 295 300

Ser Thr Glu Glu Ile Lys Ala Tyr Cys Asp Met Glu Ala Gly Gly Gly
 305 310 315 320

Gly Trp Thr Ile Ile Gln Arg Arg Glu Asp Gly Ser Val Asp Phe Gln
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Arg Thr Trp Lys Glu Tyr Lys Val Gly Phe Gly Asn Pro Ser Gly Glu
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Tyr Trp Leu Gly Asn Glu Phe Val Ser Gln Leu Thr Asn Gln Gln Arg
 355 360 365

Tyr Val Leu Lys Ile His Leu Lys Asp Trp Glu Gly Asn Glu Ala Tyr
 370 375 380

Ser Leu Tyr Glu His Phe Tyr Leu Ser Ser Glu Glu Leu Asn Tyr Arg
 385 390 395 400

Ile His Leu Lys Gly Leu Thr Gly Thr Ala Gly Lys Ile Ser Ser Ile
 405 410 415

Ser Gln Pro Gly Asn Asp Phe Ser Thr Lys Asp Gly Asp Asn Asp Lys
 420 425 430

Cys Ile Cys Lys Cys Ser Gln Met Leu Thr Gly Gly Trp Trp Phe Asp

435

440

445

Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Tyr Tyr Pro Gln Arg Gln

450

455

460

Asn Thr Asn Lys Phe Asn Gly Ile Lys Trp Tyr Tyr Trp Lys Gly Ser

465

470

475

480

Gly Tyr Ser Leu Lys Ala Thr Thr Met Met Ile Arg Pro Ala Asp Phe

485

490

495